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Form, formation, and deformation

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Chapter 4

Investigations into the cause of variation of granule size distributions produced by high shear granulation

4.1 Summary

High-shear granulation of microcrystalline cellulose (MCC) is known to result in dense, spherical pellets. However, variations in granule size distributions occur, in spite of the fact that the same recipe and process conditions are used. The aim of this study is to investigate the cause of these variations.

When starting the process, the primary particles are swept through the bowl. It was observed that sometimes particles stick to the lid, thus not participating in the initial kernel formation. Primary particles falling from the lid will consequently be layered around the kernels, instead of forming primary kernels too. This explains the broader granule size distribution.

MCC 101 was granulated with water. A comparison was made between the normal procedure where all particles were incorporated in the process immediately and a procedure in which part of the primary particles was used at the start, and after liquid addition the remaining part of the particles was added.

Results show that powder sticking on the lid indeed induces a different growth pattern. The magnitude of this problem probably depends on the scale of the experiments.

4.2 Introduction

4.2.1 High-shear granulation

In high-shear granulation blending and wet massing of a powder is accomplished through mechanical agitation by an impeller and a chopper. The impeller causes powder particles to undergo shearing and impaction forces. The chopper chops large lumps into smaller fragments [1]. This granulation technique is often used in industry because of its short processing time, the relatively low amount of liquid binder needed, and the possibility of granulating highly cohesive powders [1]. The disadvantages of this technique lie in the high shear forces, which break down fragile particles or produce particles with a too low porosity.

4.2.2 Growth regimes

Hoornaert et al. [2] describe the growth process of granules in a high-shear mixer. The initial growth stage is the nucleation regime, where wetted particles stick together and form primary nuclei. Once formed, granules can be described using the Stokes deformation number [3, 4]. This deformation number is defined as the ratio between the externally applied kinetic energy and the energy required for deformation. The small size of the primary nuclei and consequently the relatively thick binder layer results in a smaller viscous Stokes number than the critical viscous Stokes number. This means that all collisions are successful, leading to rapid growth.

When the viscous Stokes number becomes equal to the critical viscous Stokes number growth stops and the compaction stage starts. Due to the collisions a close packing is obtained. When enough binder liquid is present at the granule surface, growth by coalescence occurs. This is called the second growth stage. After a successful collision, rearrangement to a sphere may occur. Coalescence promotes the growth of larger granules. At the end of the coalescence regime, crushing and layering will be the predominant process [2].

Iveson and Litster [5] proposed a growth regime map. In this map ways of granule growth are shown, dependent on saturation and deformability. Nucleation is the first step in granulation; nuclei are formed as the binder liquid is added. Induction growth means slow consolidation followed by coalescence growth. Steady growth implies a linear increase in granule size in time. This size enlargement can be by crushing and layering or by deformation of the granule, which increases the contact surface area.

According to Scott et al. [6] the granule growth mechanism depends on the nucleation mechanism. The SMIH (immersion mechanism) leads to preferential nucleation, where nuclei do not grow much. This nucleation mechanism is promoted by pouring-on liquid; all water is immediately distributed over the powder bed. The SMDH (distribution mechanism), in which the liquid binder is distributed

over the powder, leads to preferential growth. The nuclei formed grow by coalescence with primary particles and other granules. Since coalescence promotes growth of the large granules, a bimodal granule size distribution could be obtained. This nucleation mechanism is promoted by using a melt-in liquid addition method.

4.2.3 Variation

The aim of this study was to find an explanation for the variation of granule size distributions found in the granulation of microcrystalline cellulose.

4.3 Materials and Methods

4.3.1 Materials

Microcrystalline Cellulose (Pharmatose 101, DMV International, Veghel, The Netherlands) was used in the high shear granulation process using tap water as a binding agent. In this chapter results of granulation with microcrystalline cellulose (MCC) are shown. MCC can take up water to a large extent. Water modifies the rheological properties of the wet mass by increasing the plasticity at increasing water content [7]. Fielden et al. [8] consider MCC to be a porous sponge, which can absorb a large quantity of water.

4.3.2 Methods

High shear granulation was performed in a small scale high shear mixer (MiPro 250, ProCepT, Zelzate, Belgium) using a 250 ml PMMA bowl.

Before starting a new experiment, the complete equipment was assured to be dry. The granulator was filled with maximum 24 g MCC, the impeller was set on 1000 rpm (tipspeed 3.14 m/s), the chopper on 1500 rpm. Liquid was added at 48 ml/min, unless otherwise stated. Total granulation time was 15 minutes.

The obtained granules were oven-dried overnight at 50 °C. Granule size distributions were obtained by sieving.

4.4 Results

Figure 1 shows that 3 different distributions are obtained after performing 8 identical granulation processes. It was observed during granulation, that sometimes primary powder particles were stuck on the lid. The already formed nuclei are swept around the bowl, and occasionally come into contact with the primary particles sticking to the lid. These primary particles will probably be layered around the nuclei, thus resulting in larger granules and a larger granule size distribution.

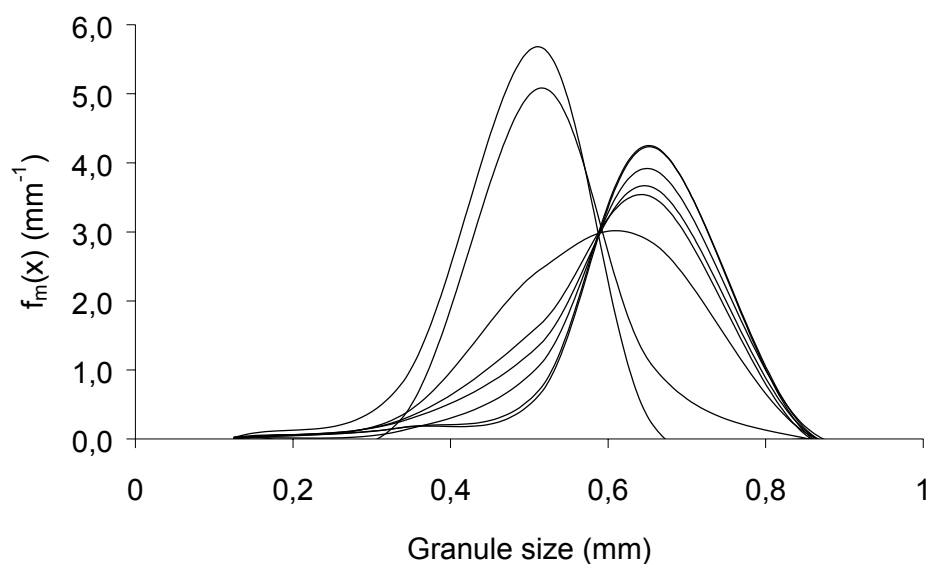


Figure 1: Size distributions obtained after eight identical experiments: 24 g MCC 101, 24 ml water 48 ml/min

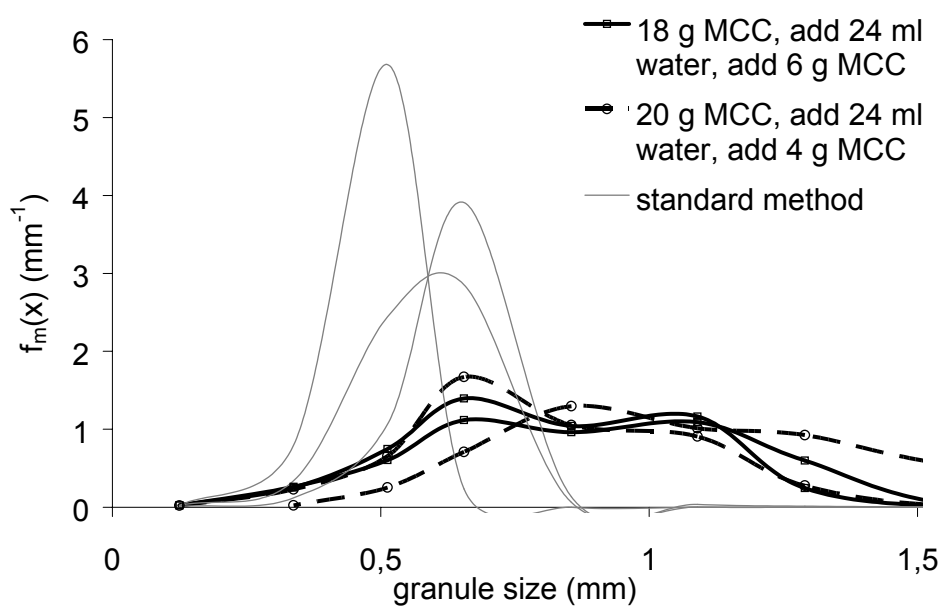


Figure 2: Size distributions obtained after modifying the granulation process by starting with only a part of the normally used amount of powder.

To mimic this effect the granulation procedure was started with only a fraction of the normally used amount of primary particles, adding water, allowing water distribution for another 30 s and adding the remaining part of the powder.

Starting with 18 g powder and adding 6 g later gives similar granule size distributions as when starting with 20 g powder and adding 4 g later, as shown in Figure 2. In this figure also the 3 size distribution categories obtained by the lines of the 'standard procedure' are shown.

The granule size distribution obtained by the modified method is much broader than the distributions obtained by the standard method. This indicates that for MCC a proper distribution of water over the primary particles is important. Layering broadens the size distribution.

Figure 3 shows that a better mimic of the occurrences during the standard granulation method is obtained when only 2 g of MCC is added during the second part of the process. Now the size distribution is close to the distributions obtained with 5 of the standard granulations.

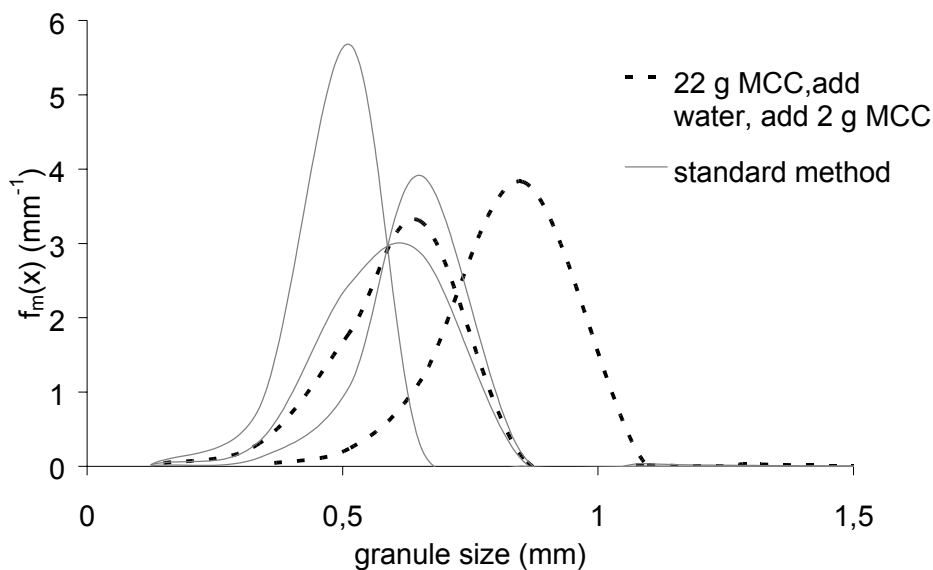


Figure 3: Size distributions obtained after modifying the standard granulation by starting with only 22 g MCC.

If indeed material is stuck to the lid, can this problem be overcome? When starting the impeller at high speed, powder is swept through the whole bowl. This can be diminished by slowing down the impeller speed.

Instead of starting with impeller speed at 1000 rpm, we started at 50 rpm. The impeller speed was turned at 1000 rpm immediately after all liquid was added,

assuring a good distribution of the liquid over the powder. Chopper speed was set unchanged at 1500 rpm. The results are shown in Figure 4. The resulting granule size distributions were similar to the smallest distributions shown in Figure 1, indicating that indeed an adequate initial spread of liquid results in a small size distribution.

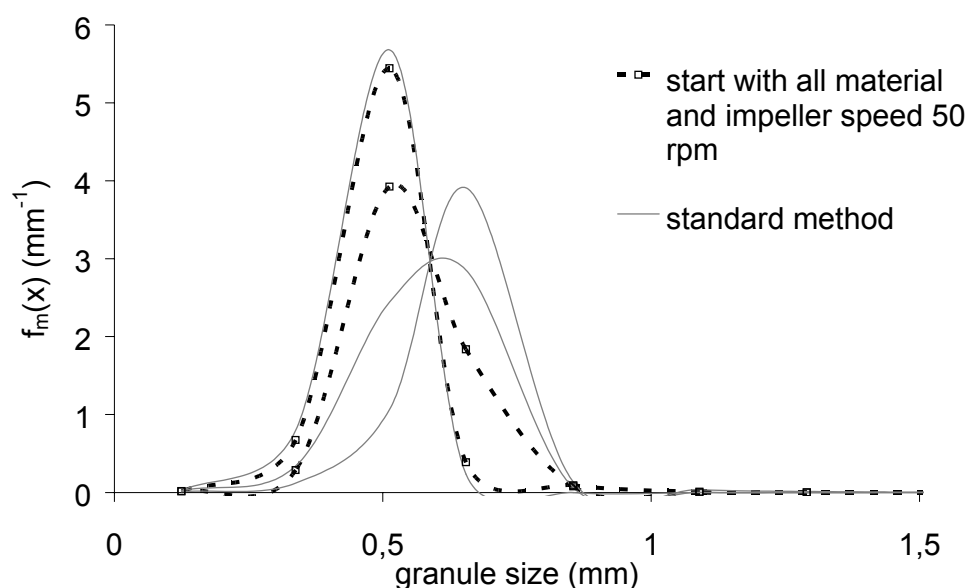


Figure 4: Size distributions obtained after modifying the standard procedure by starting with low impeller speed

In Figure 5 granule size distributions of overwet systems are shown. It shows that the more overwet the powder, the larger the granules and the broader the granule size distributions will be. The grey solid line represents one of the measurements starting with 22 g and adding 2 g MCC after liquid addition. When comparing the black solid line to the grey solid line, it is clear that the addition of 2 g of powder results in a smaller granule size distribution. However, the peak remains at the same granule size. This implies that the overwet situation determines the final size of the granules. Finally, the importance of quick water addition when using MCC was shown in Figure 6. Some materials need slow liquid addition to be able to distribute the water well. MCC on the contrary, needs fast liquid addition. The granules prepared with liquid addition rates of 48 and 96 ml/min show the smallest granule size distributions. This is in conclusion with all results shown; the speed of the water distribution determines the granule size distribution.

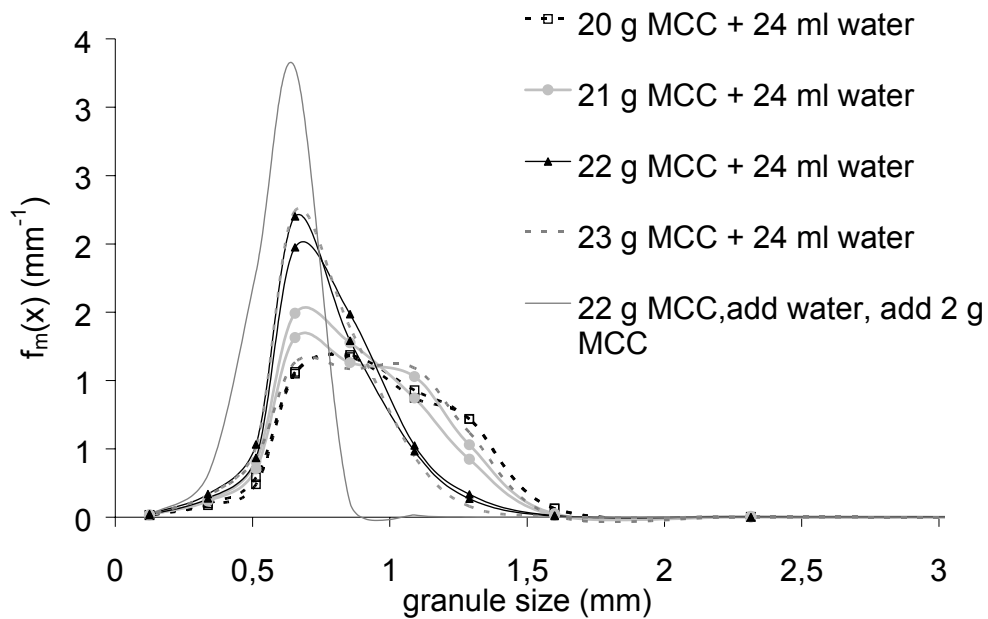


Figure 5: Size distributions of different overwet granules.

4.5 Discussion

All experiments show that a slight difference in liquid distribution over the powder bed results in differences in granule size distribution. Hoornaert et al. also show that a relatively small change in the amount of binder can change the granulation drastically [2].

The process used is probably on the edge of two different growth regimes. MCC needs a fast liquid distribution over the complete powder bed to obtain a small particle size distribution. According to Scott et al. [6] the growth regime is preferential nucleation. This fits with their ideas about the pour-on method we used.

According to the growth regime of Iveson and Litster [9], this process is called induction. Due to the good spread of liquid over the powder surface, slow consolidation followed by coalescence growth will occur. However, when not all powder is participating in the process, deviations from the smallest granule size distributions occur. Granules become larger and the granule size distribution becomes broader, depending on the amount of powder initially missing in the nucleation. This is in agreement with Holm et al, who [10] conclude that when moisture distribution is not good, large aggregates are formed due to excessive

wetting, resulting in a broad granule size distribution.

We suggest that our optimum process is the preferential nucleation [6] or induction growth [5]. However, if not all powder is incorporated in the process, but it is added later, the added powder will be layered around the nuclei formed. According to Hoornaert [2] this is a slow growing process. The process now moves towards preferential growth, due to the fact that the distribution of the binder fluid is less even. Iveson and Litster [5] call this steady growth behavior. The initially overwet powder particles are deformable due to the amount of water present, and start rapid coalescence growth. When the remaining primary particles are added, these are layered around the initial nuclei.

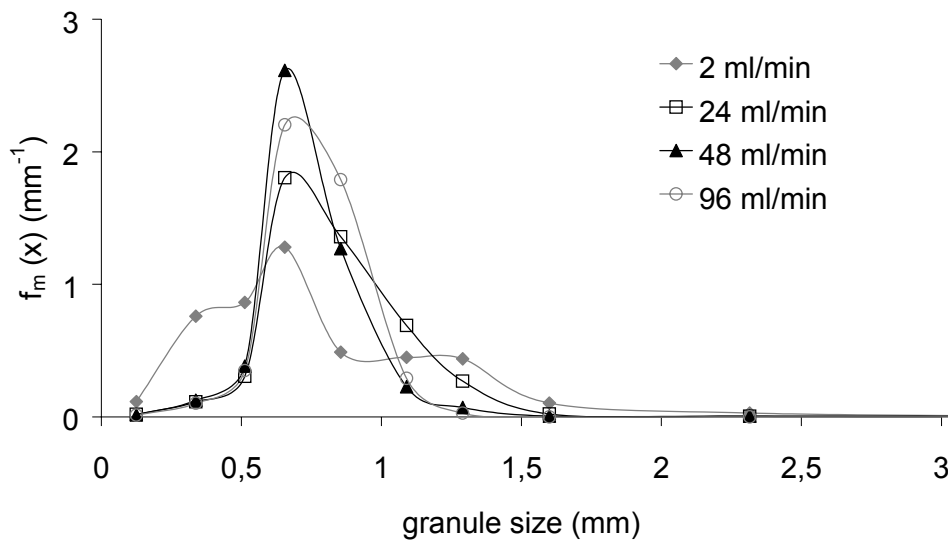


Figure 6: Size distributions showing the effect of different liquid addition speeds. These experiments were carried out using a glass bowl instead of a PMMA bowl.

4.6 Conclusions

Microcrystalline cellulose can take up large amounts of water. However, when the water is not immediately spread homogeneously over the powder bed, changes in granule size distributions are obtained. When initially not all powder is incorporated in the granulation process because it is sticking to the lid or because of overloading of the mixer, this may occur.

Although we did not use the melt-in method, we observed a change from the preferential nuclei towards the preferential growth, as described by Scott et al. [6], or a change from induction growth towards steady growth behavior as described by

Iveson and Litster [5]. This change was induced by an uneven distribution of water over the powder surface due to the primary particles which did not immediately take part in the granulation process.

4.7 References

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